Docket No. 2022(200696)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

APPLICANT:	Jeffrey P. Gillbard	CONFIMATION NO.:	8240
U.S. SERIAL NO:	10/615,158	EXAMINER:	Z.A. Fay
FILED:	July 7, 2003	GROUP:	1618

FOR: EPA AND DHA ENRICHED OMEGA-S SUPPLEMENT FOR THE TREATMENT OF DRY EYE, MEIBOMIANITIS AND ZEROSTOMIA

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

REMARKS: PRE-APPEAL BRIEF REQUEST FOR REVIEW

The following remarks support Applicant's "Pre-Appeal Brief Request for Review" filed herewith in the above-referenced application. These remarks constitute no more than five pages, and are being filed with a Notice of Appeal, thereby satisfying the requirements.

Claims 1-6 and 8-12 and 15-42 were rejected under 35 U.S.C. §103(a) as being anticipated by as allegedly being unpatentable over Ueno (US Patent 6,566,398) and Yano et al. (J. Nutrition. 130:1095-1101, 2000) in view of Troyer et al. (US Patent 6,506,412) and Schneider et al. (US Patent 6,353,022). This rejection is respectfully traversed.

Applicant respectfully requests review of the Final Office Action in the above-referenced application. No amendments are being filed with this request.

Applicant thanks the Examiner for her time and consideration during the telephonic interview on March 23, 2010. No agreement was reached.

Applicant is filing the "Pre-Appeal Brief Request for Review" based on the following clear errors and/or omissions in the Final Office Action mailed on December 29, 2009.

First Clear Error and/or Omission in the Final Office Action:

The cited references, even in combination, do not teach the instantly claimed invention.

The claims are drawn to methods of treatment of dry eye, meibomian gland inflammation, meibomian gland dysfunction, and dry mouth using a nutritional supplement containing an n-3 rich oil and an n-6 fatty acid containing oil; the nutritional supplement; and methods of manufacturing the nutritional supplement for the treatment. In the claimed supplement, the n-3 rich oil provides a high dose of each EPA (150-500 mg) and DHA (50-500 mg) providing a total of at least 200-1000 mg of omega-3 fatty acids, and the ratio of the weight of the n-6 fatty acid containing oil to the n-3 rich oil is about 1 to 3 to about 3 to 1. In certain embodiments, the supplement includes an oil soluble antioxidant such as vitamin E.

The Office Action relies on Ueno to teach "omega-3 fatty acids and omega-6 fatty acids"; and relies on Troyer for their use in the treatment of dry eye syndrome and to provide the dose of "500 mg omega-3 fatty acids" (col 3, ln 55-56 of the patent is cited). Applicant provides text of col. 3, ln 50-56. The paragraph breaks are shown as in the original.

> Omega-3 fatty acid, omega-6 fatty acid and GLA together make up about 31% of black currant seed oil. Thus, the preferred formulation contains at least about 94 mg of these three components together, and preferably contains about 235 mg of these.
>
> Omega-3 Fatty Acid
>
> Omega-3 fatty acid is an "essential" fatty acid, required in amounts of about 500 mg daily. (emphasis added)

That is, a dose of omega-3 and omega-6 fatty acids in combination are present at 94 mg to 235 mg total, whereas nutritionally, about 500 mg of omega-3 fatty acids are required daily. As black currant seed oil contains more omega-6 than omega-3 fatty acid, even at the highest suggested dose, 235 mg, Troyer could not be understood to teach the claimed doses of n-3 fatty acids.

Further, Troyer teaches a composition including *inter alia* a water soluble anti-oxidant. The instantly claimed invention is directed to an oil soluble anti-oxidant. As discussed below,

none of the references cited can provide motivation to modify Troyer to include an oil-soluble antioxidant as claimed. Applicant notes references must be considered as a whole.

Ueno teaches the administration of a fatty acid derivative, not a fatty acid, and teaches delivery at very low doses, typically as a topical solution of 0.001% or 0.0001%, or at an oral dose of 1 mg/kg (assuming a 70 kg adult, a 70 mg dose). The importance of limiting the dose to limit any undesirable side effects is specifically taught by Ueno (para bridging cols 3-4).

Applicant acknowledges that "the prior art's mere disclosure of more than one alternative does not constitute a teaching away from any of these alternatives because such disclosure does not criticize, discredit, or otherwise discourage the solution claimed." *In re Fulton*,(citation omitted, emphasis added). However, Applicant submits that Ueno criticizes, discredits, and discourages use of the doses claimed herein. Moreover, Ueno criticizes, discredits, and discourages use of the doses provided by Troyer. Therefore, there can be no motivation to make the instantly claimed invention or to combine the references as suggested.

The use of DHA, EPA, and oil soluble antioxidants is criticized, discredited, and otherwise discouraged by Yano (see pages 14-15 Oct. 14, 2009 Office Action response). Yano states "DHA, EPA and AA exhibited cytotoxicity… in high amounts" (col 1, p 1100). Yano states that EPA showed weak activity (bridging cols., p. 1100). Further, Yano states that a preincubation of 24 hours was required to observe a synergistic effect of vitamin E with DHA, whereas a water soluble antioxidants provided a more rapid effect (col. 2, p. 1100).

Schneider teaches a topical formulation for dry eye including a fatty acid derivative HETE. Schneider cannot provide any teachings regarding dosages of the instantly claimed formula. Moreover, Schneider teaches "antioxidants... protect the HETE salts from oxidation during storage. Examples… include… vitamin E and analogs thereof, ascorbic acid and derivatives, and butylated hydroxyanisole (BHA)." Therefore, the antioxidant is taught to be necessary for the stability of a synthetic compound that is neither DHA nor EPA. Further,

providing no preference for water or oil soluble antioxidants, Schneider cannot be understood to provide motivation to alter the teachings against oil-soluble antioxidants in Troyer and Yano.

The cited art cannot teach the instantly claimed invention. Troyer does not teach the claimed doses. Both Ueno and Yano teach strongly against the use of high doses, such as the doses provided by Troyer. Schneider teaches topical dosing. Yano teaches tissue culture methods an cannot provide any specific teachings relevant to dosing. Based on the teachings of the references, one cannot arrive at the instantly claimed invention.

Troyer requires water-soluble antioxidants. Yano teaches against oil soluble antioxidants. Schneider teaches antioxidants for stability of the specific compound taught and teaches no advantage of oil soluble antioxidants to motivate one to modify Yano or Troyer contrary to their teachings. Based on the teachings of the references, one cannot arrive at the instantly claimed invention.

Claims 33-37 are drawn to supplement that "consist essentially of" EPA, DHA, vitamin E, and mixed tocopherols. The cited references in any combination cannot be understood to teach a supplement consisting essentially of the elements claimed. As noted above, the fatty acid derivatives taught by Ueno are not the claimed fatty acids. Troyer teaches a composition including *inter alia* active ingredients vitamin A, vitamin B6, a source of magnesium and a water-soluble antioxidant which are not present in the claimed supplement. Schneider teaches compositions that require HETE salts as an active agent. There can be no motivation to modify the references to make formulations of Troyer and Schneider <u>not</u> including these ingredients.

The cited references in any combination cannot be understood to teach the claimed invention. The rejection should be withdrawn.

<u>Second Clear Error and/or Omission in the Final Office Action:</u>

There can be no motivation to combine the references cited as they teach against each other. References must be considered as a whole

Troyer teaches administration of fatty acids at doses of 94 mg to 235 mg. Yano teaches high doses of fatty acids are toxic in cell culture. Ueno teaches doses of fatty acid derivatives are toxic and provides a maximum dose of 1 mg/ kg, about 70 mg for an adult. Schneider teaches HETE derivative at a concentration of between 0.00001 to 0.01% w/v for a topical formulation. The references are contradictory in the use of naturally occurring or derivatized fatty acids. The references are contradictory in the doses that should be administered.

Ueno and Schneider teach fatty acid derivatives. Ueno teaches fatty acid derivatives broadly as being useful for the treatment of dry eye, but demonstrates the utility of only one. Schneider teaches that treatment of dry eye can only be accomplished with specific fatty acid derivatives, particularly HETEs (col. 3, ln 21-48).

Troyer and Yano discuss the use of naturally occurring fatty acids DHA and EPA. Troyer teaches compositions that include EPA and DHA with other components for treatment of dry eye. Yano teaches that EPA and DHA are not active in assays provided.

When taken as a whole, the references can only be understood to contradict each other and cause confusion rather than providing any obvious path forward to any invention.

Applicant submits that all of the claims under final rejection are in condition for allowance and should be allowed, and that the Final Office Action should be withdrawn.

Respectfully submitted,

Date: March 26, 2010

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